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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,911	08/09/2006	Susan Elizabeth Bove	PC32145A	8818

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GLOBAL PATENT DEPARTMENT
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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
07/15/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/588,911	BOVE ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *3-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 6-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claim 13 has been canceled in the amendment filed 5/28/09. Claims 3-5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected claims. Amended claims 1, 11-12 (5/28/09), and previously presented claims 2, 6-10, are pending and under consideration by the Examiner.

2. Receipt of Applicant's arguments and amendments filed on 5/28/2009 is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 5/28/09:

(i) the objection to the title of the invention;

(ii) the rejection of claims 13 under 35 U.S.C. 101; and

(iii) the rejection of claim 8, under 35 U.S.C. 112, first paragraph;

(iv) the rejection of claims 1-2, 6-13, under 35 U.S.C. 112, second paragraph;

(v) the rejection of claims 1-2, 6-7, 9-13, under 35 U.S.C. § 103 as being unpatentable over Kishimoto et al (US Patent No. 5,888,510) in view of Raynauld et al. (2003);

(vi) the rejection of claim 7 under 35 U.S.C. 103(a) as being unpatentable over Kishimoto et al. (US Patent No. 5,888,510) in view of Raynauld et al. (2003) as applied to claims 1-2, 6, 9-13, above, and further in view in of Queen et al. (U.S. Patent No. 5,530,101).

4. Applicant's arguments filed on 5/28/2009 have been fully considered and were persuasive. The new issues are stated below.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5a. Claims 1-2, 6, 9-10, are rejected under 35 U.S.C. § 103 as being unpatentable over Kishimoto et al (US Patent No. 5,888,510) in view of Kaneko et al. (2000).

Kishimoto et al. teach a method for inhibiting synovial cell growth by administering to a patient polyclonal or monoclonal antibodies to IL-6 (see claims 1-4) and also teach a method of treating chronic rheumatoid arthritis by administering to a patient IL-6 antagonists including polyclonal or monoclonal antibodies to the IL-6 receptor (see claims 1-11; Example 2, columns 13-14, column 7, 42-48). Kishimoto also teaches that IL-6 antibody binds to IL-6 and inhibits the binding between IL-6 and the IL-6 receptor and thus blocks IL-6 signal transduction, inhibiting inflammation which is IL-6 biological activity (see column 3, lines 53-60). Therefore, Kishimoto discloses that if a cytokine causes a disease, an antibody to the cytokine will block the signal transduction by the cytokine, inhibit the cytokines biological activity and has an alleviating and therapeutic effect on the symptoms of the disease (see column 3, lines 41-52). However, Kishimoto does not disclose a method of treating osteoarthritis by administering an IL-6 antibody.

Kaneko et al teach that significantly higher concentrations of inflammatory cytokine IL-6 levels were found in serum and synovial fluid of patients with osteoarthritis (see abstract, column 1, lines 7-10; Figure 2, page 74; page 78, column 1, last 9 lines, and column 2, first 7 lines). Kaneko et al. do not disclose a method of administering IL-6 antibodies to treat osteoarthritis in a patient.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art, from the method of Kishimoto to administer IL-6 antibodies to a patient for the treatment of osteoarthritis to obtain the known functions and advantages thereof as per the teachings of Kishimoto et al because Kaneko et al teach that elevated levels of the inflammatory cytokine IL-6 are found in osteoarthritic patients. Therefore, a person of ordinary skill in the art would have been

motivated to administer the IL-6 antibodies of Kishimoto et al., in the treatment of osteoarthritis because Kishimoto et al teach the properties of IL-6 antibodies and Kaneko et al provides the motivation to administer IL-6 antibodies to inhibit the inflammation caused by IL-6. Therefore, treatment of patients with IL-6 antibodies would be expected to relieve the symptoms of osteoarthritis. Administration of IL-6 antibodies would be effective therapy for osteoarthritis because Kishimoto teaches that administration of IL-6 antibodies reduces inflammation caused by IL-6 in patient populations with rheumatoid arthritis. Both rheumatoid arthritis and osteoarthritis are chronic inflammatory diseases and one of skill in the art would have expected success in reducing inflammation caused by IL-6 in osteoarthritic patients by administering IL-6 antibodies. Furthermore, it would have been obvious to one of skill in the art to modify the method of Kishimoto by administering the antibody whether interarticularly or intravenously to achieve the most efficacious mode of administration. Therefore, the teachings of both Kishimoto and Kaneko translate into a benefit for administering IL-6 antibodies for treating patients with osteoarthritis. Therefore, the teachings of both Kishimoto and Kaneko render obvious instant claims 1-2, 6, 9-10.

5b. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kishimoto et al (US Patent No. 5,888,510) in view of Kaneko et al. (2000) as applied to claims 1-2, 6, 9-10, above, and further in view of Queen et al. (U.S. Patent No. 5,530,101).

The disclosures of Kishimoto et al and Kaneko et al have been set forth above (see paragraph 5a above). However, neither Kishimoto et al nor Kaneko et al disclose a method of administering anti-human IL-6 antibodies for treatment of osteoarthritis.

Queen et al., (column 13, lines 5-65) teaches the humanization of monoclonal antibodies,

as well as the issues involved in designing a humanized antibody that retains high affinity for its antigen. Queen et al., (column 17, lines 31-43) further teaches the production of antibody fragments, including the Fab fragment.

Therefore, at the time the invention was made, it would have been prima facie obvious to a person of ordinary skill in the art to administer as taught by Queen et al, humanized monoclonal antibodies to IL- 6 for treatment of osteoarthritis in a patient in a method as taught by Kishimoto in view of Kaneko et al. The motivation for doing so would have been the decreased immunogenicity of humanized antibodies when injected into humans, while the humanized antibodies retain their affinity for their epitope (Queen et al., (column 2, lines 5-8)).

5c. Claims 11-12, are rejected under 35 U.S.C. § 103 as being unpatentable over Kishimoto et al (US Patent No. 5,888,510) in view of Kaneko et al. (2000) and Karim et al. (US Patent No. 5,888,510).

The disclosures of Kishimoto et al and Kaneko et al have been set forth above (see paragraph 5a above). However, neither Kishimoto et al nor Kaneko et al disclose a method of administering IL-6 antibodies and celecoxib or ibuprofen for treatment of osteoarthritis.

Karim et al teach administration of agents, such as celecoxib or ibuprofen, for fast relief of pain in osteoarthritic patients, is clinically effective for relief of symptoms of pain from osteoarthritis (see column 1, lines 55-65;column 2, lines 33-45).

It would have been *prima facie* obvious to one having ordinary skill in the art, from the teachings of Kishimoto and Kaneko, to administer IL-6 antibodies to patients together with

celecoxib or ibuprofen for the treatment of osteoarthritis as taught by Karim et al to obtain the known functions and advantages thereof as per the teachings of Karim et al and Kishimoto et al. Therefore, to administer IL-6 antibodies of Kishimoto et al., in the treatment of osteoarthritis together with administration of celecoxib or ibuprofen as shown by the teachings of Karim et al., would be obvious because all three agents are used for the treatment of IL-6 induced chronic inflammation which includes chronic inflammatory diseases such as rheumatoid arthritis and osteoarthritis. One would have been motivated to administer IL-6 antibodies together with agents for fast pain relief because Kishimoto et al teach administration of IL-6 antibodies and Karim et al provides the motivation to administer celecoxib or ibuprofen to relieve the pain caused by the inflammation which is caused by IL-6. Therefore, treatment with these agents would be expected to relieve all the symptoms of osteoarthritis. Administration of these agents would be effective therapy for osteoarthritis because IL-6 antibodies reduce inflammation caused by IL-6 and celecoxib or ibuprofen work in both types of patients with rheumatoid arthritis and osteoarthritis to obtain relief from pain. Therefore, the teachings of Kishimoto, Kaneko and Karim translate into a benefit for administering IL-6 antibodies and celecoxib or ibuprofen for treating patients with osteoarthritis.

Conclusion

No claim is allowed.

Claims 1-2, 6-12, are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Prema Mertz/
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Art Unit 1646